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# Bootstraps of sums of independent but not identically distributed stochastic processes

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## Abstract

A central limit theorem is developed for sums of independent but not identically distributed stochastic processes multiplied by independent real random variables with mean zero. Weak convergence of the Hoffmann–Jørgensen–Dudley type, as described in van der Vaart and Wellner (Weak Convergence and Empirical Processes, Springer, New York, 1996), is utilized. These results allow Monte Carlo estimation of limiting probability measures obtained from application of Pollard’s (Empirical Processes: Theory and Applications, IMS, Hayward, CA, 1990) functional central limit theorem for empirical processes. An application of this theory to the two-parameter Cox score process with staggered entry data is given for illustration. For this process, the proposed multiplier bootstrap appears to be the first successful method for estimating the associated limiting distribution. The results of this paper compliment previous bootstrap and multiplier central limit theorems for independent and identically distributed empirical processes.

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## 1. Introduction

Pollard’s [10] functional central limit theorem, Theorem 10.6, for independent but not identically distributed random processes has proven quite useful in establishing

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weak convergence results for several difficult statistical problems. Among other benefits, this general approach allows the practical use of nonidentically distributed regression covariates—as happens when covariates are assumed fixed or when a biased coin study design (see [16], for example) is used—as well as independent but nonidentically distributed censoring times (which can also occur as a design feature). Two recent examples of research utilizing Pollard’s approach include the two-parameter Cox score process (particularly as studied in [3]) and the semiparametric accelerated failure time models of Lin et al. [8].

A major challenge for doing inference in these settings is that the limiting distributions are frequently very difficult to characterize. Unfortunately, the nonidentically distributed nature of the data precludes the use of the usual bootstrap and closely related multiplier central limit theorems for sums of independent and identically distributed empirical processes [5,7,9,11,12]. For a superb overview of these results, see [15, Chapters 2.9 and 3.6] (hereafter abbreviated VW). Extending these results to independent but not identically distributed processes appears to be nontrivial: this extension is the goal of the present paper.

The approach we take for obtaining bootstrap results for the independent but nonidentically distributed setting is motivated by Pollard’s [10] functional central limit theorem, although there are a number of other possible directions suggested by functional central limit theorems either based on random and uniform-entropy [1] or based on bracketing [2] as discussed in Chapter 2.11 of VW. A promising, related approach based on uniformly integrable entropy is described in [17]. Although the entropy conditions of these theorems are generally not as strong as the manageability condition used in Pollard’s theorem, an important benefit is that total boundedness of the index set for the limiting stochastic process is a consequence—not a condition—of the theorem. Moreover, the approach suggested by Pollard’s theorem appears to lend itself most naturally to the kind of multiplier functional central limit theorem we are seeking while requiring assumptions which appear to be reasonably easy to verify in many practical settings.

Because of measurability issues which arise occasionally in statistics, particularly in counting process settings, we take the Hoffmann–Jørgensen–Dudley (hereafter abbreviated HJD) approach to weak convergence which utilizes outer measure as outlined extensively in the first section of VW.

In Section 2, we provide some necessary background, state Pollard’s functional central limit theorem, and then introduce sufficient measurability conditions. The main theoretical results for the multiplier bootstraps are then given in Section 3. The paper concludes in Section 4 with an application of these results to the two-parameter Cox score process.

## 2. Weak convergence and measurability

We are interested in estimating the limiting distribution of sums of the form  $\sum_{i=1}^{m_n} f_{ni}(\omega, t)$ , where the real-valued stochastic processes  $\{f_{ni}(\omega, t), t \in T, 1 \leq i \leq m_n\}$ ,

for  $n \geq 1$ , are independent within rows on the probability space  $\{\Omega, \mathcal{W}, \Pi\}$  for arbitrary index set  $T$ . We will assume the usual pointwise measurability of these stochastic processes, i.e.,  $f_{ni}(\cdot, t) : \Omega \mapsto \mathfrak{R}$  is measurable for each  $t \in T$ ,  $1 \leq i \leq m_n$ , and all  $n \geq 1$ . Consistent with the notation in VW, we will use  $E^*$  and  $P^*$  to denote outer expectation and outer probability, respectively, in addition to the usual expectation and probability,  $E$  and  $P$ , when measurability requirements are satisfied. For a map  $h$  from a probability space to  $\mathfrak{R}$ , we will use  $h^*$  to denote a measurable cover function in accordance with Lemma 1.2.1 of VW. For the computation of outer expectations, independence will always be understood to imply that the projections of the probability spaces involved for fixed  $n$  are products of the probability spaces corresponding to each independent process. Sometimes function arguments or subscripts will be suppressed for notational clarity. Let  $\ell^\infty(T)$  denote the space of all uniformly bounded, real functions on  $T$ , and endow  $\ell^\infty(T)$  with the uniform metric. Also, for any pseudo-metric  $v$  on  $T$ , let

$$U_v(T) \equiv \{z \in \ell^\infty(T) : z \text{ is uniformly } v\text{-continuous}\}.$$

We need the following definition of manageability (Definition 7.9 of Pollard [10], with minor modification). First, for any set  $A \in \mathfrak{R}^m$ , let  $D_m(x, A)$  be the largest  $k$  such that there exist  $k$  points in  $A$  with the smallest Euclidean distance between any two distinct points being greater than  $x$  (this is the *packing number* described in [10, Definition 3.3]). Also let  $\mathcal{F}_{n\omega} \equiv \{[f_{n1}(\omega, t), \dots, f_{nm_n}(\omega, t)] \in \mathfrak{R}^{m_n} : t \in T\}$ ; and for any vectors  $\mathbf{u}, \mathbf{v} \in \mathfrak{R}^m$ ,  $\mathbf{u} \odot \mathbf{v} \in \mathfrak{R}^m$  is the pointwise product and  $\|\mathbf{u}\|$  is the Euclidean distance.

**Manageability:** Call a triangular array of processes  $\{f_{ni}(\omega, t)\}$  *manageable*, with respect to the (nonnegative) envelopes  $\mathbf{F}_n(\omega) \equiv [F_{n1}(\omega), \dots, F_{nm_n}(\omega)] \in \mathfrak{R}^{m_n}$  if there exists a deterministic function  $\lambda$  (the *capacity bound*) for which

- (i)  $\int_0^1 \sqrt{\log \lambda(x)} dx < \infty$ ,
- (ii) there exists  $N \subset \Omega$  such that  $P^*(N) = 0$  and for each  $\omega \notin N$ ,

$$D_{m_n}(x \|\mathbf{\alpha} \odot \mathbf{F}_n(\omega)\|, \mathbf{\alpha} \odot \mathcal{F}_{n\omega}) \leq \lambda(x),$$

for  $0 < x \leq 1$ , all vectors  $\mathbf{\alpha} \in \mathfrak{R}^{m_n}$  of nonnegative weights, all  $n \geq 1$ , and where  $\lambda$  does not depend on  $\omega$  or  $n$ .

We now state Pollard's Functional Central Limit Theorem for the stochastic process

$$X_n(\omega, t) \equiv \sum_{i=1}^{m_n} [f_{ni}(\omega, t) - Ef_{ni}(\cdot, t)].$$

**Theorem 1.** Suppose the processes from the triangular array  $\{f_{ni}(\omega, t), t \in T\}$  are independent within rows and satisfy

- (A) the  $\{f_{ni}\}$  are manageable, as defined above, with envelopes  $\{\mathbf{F}_{ni}\}$  which are also independent within rows;

- (B)  $H(s, t) = \lim_{n \rightarrow \infty} EX_n(s)X_n(t)$  exists for every  $s, t \in T$ ;  
 (C)  $\limsup_{n \rightarrow \infty} \sum_{i=1}^{m_n} EF_{ni}^2 < \infty$ ;  
 (D)  $\lim_{n \rightarrow \infty} \sum_{i=1}^{m_n} EF_{ni}^2 \{F_{ni} > \varepsilon\} = 0$  for each  $\varepsilon > 0$ , where  $\{A\}$  is the indicator of  $A$ ;  
 (E)  $\rho(s, t) = \lim_{n \rightarrow \infty} \rho_n(s, t)$ , where

$$\rho_n(s, t) \equiv \left( \sum_{i=1}^{m_n} E|f_{ni}(\cdot, s) - f_{ni}(\cdot, t)|^2 \right)^{1/2},$$

exists for every  $s, t \in T$ , and for all deterministic sequences  $\{s_n\}$  and  $\{t_n\}$  in  $T$ , if  $\rho(s_n, t_n) \rightarrow 0$  then  $\rho_n(s_n, t_n) \rightarrow 0$ .

Then, provided we have sufficient measurability,

- (i)  $T$  is totally bounded under the  $\rho$  pseudometric;  
 (ii)  $X_n$  converges HJD weakly on  $\ell^\infty(T)$  to a tight mean zero Gaussian process  $X$  concentrated on  $U_\rho(T)$ , with covariance  $H(s, t)$ .

The proof is given in [10, Chapter 10]. The following condition on triangular arrays provides sufficient measurability for Theorem 1 (and for later results):

*Almost measurable Suslin:* Call a triangular array  $\{f_{ni}(\omega, t), t \in T\}$  *almost measurable Suslin* (AMS) if for all  $n \geq 1$ , there exists a Suslin topological space  $T_n \subset T$  with Borel sets  $\mathcal{B}_n$  such that

$$(i) \quad P^* \left( \sup_{t \in T} \inf_{s \in T_n} \sum_{i=1}^{m_n} (f_{ni}(\omega, s) - f_{ni}(\omega, t))^2 > 0 \right) = 0,$$

- (ii) For  $i = 1, \dots, m_n$ ,  $f_{ni} : \Omega \times T_n \mapsto \mathfrak{R}$  is  $\mathcal{W} \times \mathcal{B}_n$ -measurable.

**Lemma 1.** *If the triangular array  $\{f_{ni}(\omega, t), t \in T\}$  is AMS, then it is sufficiently measurable for the conclusions of Theorem 1 to hold and conditions (C) and (D) can be weakened to*

- (C')  $\limsup_{n \rightarrow \infty} \sum_{i=1}^{m_n} E^* F_{ni}^2 < \infty$ ;  
 (D')  $\lim_{n \rightarrow \infty} \sum_{i=1}^{m_n} E^* F_{ni}^2 \{F_{ni} > \varepsilon\} = 0$  for each  $\varepsilon > 0$ ;

**Remark 1.** While  $F_{ni}(\omega)$  is often taken to be  $\sup_{t \in T} |f_{ni}(\omega, t)|$ , and would thus be measurable as a consequence of the AMS assumption, there are many settings where other choices of envelopes would be more appropriate, such as when the  $\{f_{ni}\}$  are the differences between two other manageable processes, e.g.,  $f_{ni} = g_{ni} - h_{ni}$ ,  $i = 1, \dots, m_n$ ,  $n \geq 1$ . In this example, the envelope  $\sup_{t \in T} |g_{ni}(\omega, t)| + \sup_{t \in T} |h_{ni}(\omega, t)|$  will frequently work better than  $\sup_{t \in T} |f_{ni}(\omega, t)|$ ,  $i = 1, \dots, m_n$ ,  $n \geq 1$ , in establishing weak convergence.

**Proof of Lemma 1.** For every  $\eta, \tau > 0$ , let

$$f_{ni}^{\eta\tau}(\omega, t) \equiv f_{ni}(\omega, t) \{ (F_{ni}(\omega) \{ F_{ni}(\omega) > \eta \})^* > \tau \}.$$

The  $\{f_{ni}^{\eta\tau}(\omega, t)\}$  are clearly measurable stochastic processes. The usual symmetrization arguments (see for example Theorem 2.2 of Pollard [10]) yield for any convex, increasing  $\Phi$ ,

$$E^* \Phi \left( \sup_{t \in T} \left| \sum_{i=1}^{m_n} [f_{ni}^{\eta\tau}(\omega, t) - E f_{ni}^{\eta\tau}(\cdot, t)] \right| \right) \leq E^* \Phi \left( 2 \sup_{t \in T} \left| \sum_{i=1}^{m_n} \sigma_i f_{ni}^{\eta\tau}(\omega, t) \right| \right),$$

where  $\sigma_i, i \geq 1$ , are independent Rademacher random variables (taking on the values  $\{-1, 1\}$  with equal probability). Furthermore, the AMS assumption gives us that

$$E^* \Phi \left( 2 \sup_{t \in T} \left| \sum_{i=1}^{m_n} \sigma_i f_{ni}^{\eta\tau}(\omega, t) \right| \right) = E \Phi \left( 2 \sup_{t \in T_n} \left| \sum_{i=1}^{m_n} \sigma_i f_{ni}^{\eta\tau}(\omega, t) \right| \right);$$

and we can now use Fubini's Theorem to exchange the order of integration so that Pollard's [10] inequality 7.10 can be applied, for  $\Phi(\cdot) = |\cdot|$ , to obtain

$$\begin{aligned} E^* \sup_{t \in T} \left| \sum_{i=1}^{m_n} [f_{ni}^{\eta\tau}(\omega, t) - E f_{ni}^{\eta\tau}(\cdot, t)] \right| \\ \leq k \left( E^* \sum_{i=1}^{m_n} F_{ni}^2(\cdot) \{ (F_{ni}(\cdot) \{ F_{ni}(\cdot) > \eta \})^* > \tau \} \right)^{1/2}, \end{aligned}$$

where  $k < \infty$  does not depend on  $n$ . However,

$$\begin{aligned} \limsup_{n \rightarrow \infty} \sum_{i=1}^{m_n} E^* F_{ni}^2(\cdot) \{ (F_{ni}(\cdot) \{ F_{ni}(\cdot) > \eta \})^* > \tau \} \\ \leq \limsup_{n \rightarrow \infty} \sum_{i=1}^{m_n} E^* F_{ni}^2(\cdot) \{ F_{ni}(\cdot) \leq \eta \} \{ (F_{ni}(\cdot) \{ F_{ni}(\cdot) > \eta \})^* > \tau \} \\ \leq \eta \tau^{-1} \limsup_{n \rightarrow \infty} \left( \sum_{i=1}^{m_n} E^* F_{ni}^2(\cdot) \right)^{1/2} \left( \sum_{i=1}^{m_n} E^* F_{ni}^2(\cdot) \{ F_{ni}(\cdot) > \eta \} \right)^{1/2} \\ = 0. \end{aligned}$$

(Note that we must be extra careful in these inequalities on account of the properties of outer measure.)

The same result holds true if we replace  $\eta$  and  $\tau$  with sequences  $\eta_n$  and  $\tau_n$  going to zero slowly enough. Thus, without loss of generality, we can assume  $(F_{ni} \{ F_{ni} > \eta_n \})^* \leq \tau_n$ . Furthermore,

$$\begin{aligned} F_{ni}^* &\leq (F_{ni} \{ F_{ni} \leq \eta_n \})^* + (F_{ni} \{ F_{ni} > \eta_n \})^* \\ &\leq \eta_n + \tau_n, \end{aligned}$$

and we can therefore assume, without loss of generality, that  $F_{ni}$  is measurable with  $F_{ni}(\omega) \leq \varepsilon_n$  for some sequence  $\varepsilon_n$  going to zero as  $n \rightarrow \infty$ ,  $i = 1, \dots, m_n$ ,  $n \geq 1$ , for all  $\omega \notin N$ , where  $P^*(N) = 0$ .

If we now denote  $h_{ni}(\omega, s, t) \equiv f_{ni}(\omega, s) - f_{ni}(\omega, t)$ , the AMS condition again gives us enough measurability that we can use Fubini's Theorem at the appropriate juncture to obtain

$$\limsup_{n \rightarrow \infty} E^* \sup_{s, t \in T} \left| \sum_{i=1}^{m_n} h_{ni}^2(\omega, s, t) - E h_{ni}^2(\cdot, s, t) \right|^2 = 0.$$

Pollard's arguments establishing that  $T$  is totally bounded under the  $\rho$  pseudo-metric can now be applied. Now, for any sequence  $r_n$  going to zero, let

$$u_n(\omega) = r_n + \sup_{s, t \in T: \rho(s, t) < r_n} |\rho_n(s, t) - \rho(s, t)| + \sup_{s, t \in T_n} |\hat{\rho}_n(\omega, s, t) - \rho_n(s, t)|,$$

where

$$\hat{\rho}_n^2(\omega, s, t) \equiv \sum_{i=1}^{m_n} (f_{ni}(\omega, s) - f_{ni}(\omega, t))^2.$$

Based on previous arguments,  $u_n$  is measurable and goes to zero in probability. Now, for any  $p: 1 \leq p < \infty$ ,

$$\begin{aligned} E^* & \left( \sup_{s, t \in T: \rho(s, t) < r_n} \left| \sum_{i=1}^{m_n} \sigma_i [f_{ni}(\omega, s) - f_{ni}(\omega, t)] \right|^p \right) \\ & \leq E \left( \sup_{s, t \in T_n: \hat{\rho}_n(\omega, s, t) < u_n(\omega)} \left| \sum_{i=1}^{m_n} \sigma_i [f_{ni}(\omega, s) - f_{ni}(\omega, t)] \right|^p \right); \end{aligned}$$

and measurability again permits us to apply Fubini's theorem as well as Pollard's inequality (10.8) to obtain that the right-hand side has expectation bounded by

$$E\{ \|F_n(\omega)\|^p \Gamma(u_n(\omega)) / \|2F_n(\omega)\| \},$$

where  $\Gamma$  is a continuous, increasing function with  $\Gamma(0) = 0$ . Thus we can utilize the remaining arguments of Pollard's proof, and the results follow.  $\square$

The following condition is stronger than AMS but is easier to verify for many statistical applications:

*Separability:* Call a triangular array of processes  $\{f_{ni}(\omega, t), t \in T\}$  *separable* if for every  $n \geq 1$ , there exists a countable subset  $T_n \subset T$  such that

$$P^* \left( \sup_{t \in T} \inf_{s \in T_n} \sum_{i=1}^{m_n} (f_{ni}(\omega, s) - f_{ni}(\omega, t))^2 > 0 \right) = 0.$$

**Lemma 2.** *If the triangular array of stochastic processes  $\{f_{ni}(\omega, t), t \in T\}$  is separable, then it is AMS.*

**Proof.** The discrete topology applied to  $T_n$  makes it into a Suslin topology by countability, with resulting Borel sets  $\mathcal{B}_n$ . For  $i = 1, \dots, m_n$ ,  $f_{ni} : \Omega \times T_n \mapsto \mathfrak{R}$  is  $\mathcal{W} \times \mathcal{B}_n$ -measurable since, for every  $\alpha \in \mathfrak{R}$ ,

$$\{(\omega, t) \in \Omega \times T_n : f_{ni}(\omega, t) > \alpha\} = \bigcup_{s \in T_n} \{(\omega, s) : f_{ni}(\omega, s) > \alpha\},$$

and the right-hand side is a countable union of  $\mathcal{W} \times \mathcal{B}_n$ -measurable sets.  $\square$

The foregoing measurable Suslin condition is closely related to the definition given in Example 2.3.5 of VW while the definition of separable arrays is similar in spirit to the definition given in Section 2.3.3 of VW for sums of stochastic processes. The modifications of these definitions presented in this paper have been made to accommodate nonidentically distributed arrays for a broad scope of statistical applications; however, finding the best measurability conditions is not the primary goal.

### 3. Main results

We now present two multiplier central limit theorems that permit approximate inference on  $X_n$  in spite of the complexity of the limiting distribution. The second theorem establishes consistency of a multiplier bootstrap closely related to what some authors call a wild bootstrap [12]. The first theorem is a necessary intermediate step. Let  $\{z_i, i \geq 1\}$  be a sequence of random variables satisfying

(F) The  $\{z_i\}$  are independent and identically distributed, on the probability space  $\{\Omega_z, \mathcal{W}_z, \Pi_z\}$ , with mean zero and variance 1.

Denote  $\mu_{ni}(t) \equiv Ef_{ni}(\cdot, t)$ . The array of stochastic processes  $\{z_i[f_{ni}(\omega, t) - \mu_{ni}(t)], t \in T\}$ , for  $n \geq 1$ , can now be defined on the product probability space  $\{\Omega, \mathcal{W}, \Pi\} \times \{\Omega_z, \mathcal{W}_z, \Pi_z\}$ . We first consider weak convergence of the multiplier process

$$\tilde{X}_{nc\omega}(t) \equiv \sum_{i=1}^{m_n} z_i[f_{ni}(\omega, t) - \mu_{ni}(t)].$$

For a metric space  $\{D, d\}$ , let  $BL_1(D)$  be the space of real-valued functions on  $D$  with Lipschitz norm bounded by 1, i.e., for any  $f \in BL_1(D)$ ,  $\sup_{x \in D} |f(x)| \leq 1$  and  $|f(x) - f(y)| \leq d(x, y)$  for all  $x, y \in D$ . As described in the discussion following Theorem 1.12.2 of VW, we know that  $X_n$  converges HJD weakly to  $X$  on  $D$ , where  $X$  is Borel Measurable and separable, if and only if

$$\sup_{f \in BL_1(D)} |E^*f(X_n) - Ef(X)| \rightarrow 0$$

as  $n \rightarrow \infty$ . One of the appealing features of this approach to weak convergence is that it nicely resolves certain measurability problems for multiplier processes as is done, for example, in Theorem 2.9.6 of VW. In the following theorem, let  $E_z$  denote taking expectation over the multipliers  $\{z_i\}$  conditional on the data  $\{f_{ni}\}$ .

**Theorem 2.** Suppose the triangular array of stochastic processes  $\{f_{ni}(\omega, t), t \in T\}$  satisfies the conditions of Theorem 1 and is AMS. Suppose also that the sequence of random variables  $\{z_i\}$  satisfies condition (F) and is independent of  $\{f_{ni}\}$ . Then the conclusions of Theorem 1 obtain,  $\hat{X}_{n\omega}$  is asymptotically measurable, and

$$\sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\hat{X}_{n\omega}) - Eh(X)| \rightarrow 0 \quad (3.1)$$

in outer probability as  $n \rightarrow \infty$ .

**Remark 2.** Theorem 2 implies that the multiplier process conditional on the data,  $\{f_{ni}\}$ , accurately characterizes the distribution of sample paths of  $X$  and, if the  $\{\mu_{ni}\}$  were known, could thus be used for inference on the limiting distribution of  $X_n$ .

In order to be able to take advantage of these results in practice, we will need estimators  $\hat{\mu}_{ni}$  of  $\mu_{ni}$ ,  $i = 1, \dots, m_n$ ,  $n \geq 1$ . We can then use Monte Carlo methods to estimate the conditional distribution (given  $\omega$ ) of the stochastic process

$$\hat{X}_{n\omega}(t) \equiv \sum_{i=1}^{m_n} z_i [f_{ni}(\omega, t) - \hat{\mu}_{ni}(\omega, t)].$$

To this end, we have the following:

**Theorem 3.** Suppose the triangular array  $\{f_{ni}\}$  and the sequence  $\{z_i, i \geq 1\}$  satisfy the conditions of Theorem 2. Suppose also that the array of estimators  $\{\hat{\mu}_{ni}(\omega, t), t \in T, 1 \leq i \leq m_n, n \geq 1\}$  is AMS and satisfies the following:

- (G)  $\sup_{t \in T} \sum_{i=1}^{m_n} [\hat{\mu}_{ni}(\omega, t) - \mu_{ni}(t)]^2$  converges to zero in outer probability as  $n \rightarrow \infty$ ;
- (H) the stochastic processes  $\{\hat{\mu}_{ni}(\omega, t)\}$  are manageable with envelopes  $\{\hat{F}_{ni}(\omega)\}$ ;
- (I)  $k \vee \sum_{i=1}^{m_n} [\hat{F}_{ni}(\omega)]^2$  converges to  $k$  in outer probability as  $n \rightarrow \infty$ , for some  $k < \infty$ .

Then the conclusions of Theorems 1 and 2 obtain,  $\hat{X}_{n\omega}$  is asymptotically measurable, and

$$\sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\hat{X}_{n\omega}) - Eh(X)| \rightarrow 0 \quad (3.2)$$

in outer probability as  $n \rightarrow \infty$ .

**Remark 3.** The above results essentially amount to weak convergence of  $\hat{X}_{n\omega}$ , given  $\omega$ , to  $X$ . For example, suppose  $A$  is Borel subset of  $\ell^\infty(T)$  with the property that  $P\{X \in \text{boundary of } A\} = 0$ ; then  $P\{\hat{X}_{n\omega} \in A | \omega\}^*$  converges in outer probability to  $P\{X \in A\}$ , as  $n \rightarrow \infty$ . This follows from Lemma 1.9.2 and Theorem 1.12.2 of VW combined with the Portmanteau Theorem (Theorem 1.3.4 of VW).

We need the following lemma before presenting the proofs of these theorems:



**Lemma 3.** Let  $\{Y_{ni}, i = 1, \dots, m_n, n \geq 1\}$  be a triangular array of mean zero real random vectors in  $\mathfrak{R}^d$ , independent within rows; and let  $\{z_i, i \geq 1\}$  satisfy condition (F) and be independent of  $\{Y_{ni}\}$ . Suppose also that

- (a)  $\lim_{n \rightarrow \infty} \sum_{i=1}^{m_n} E Y_{ni} Y_{ni}^t = V_0 < \infty$ , where superscript  $t$  denotes transpose;  
 (b) for every  $\eta > 0$ ,

$$\limsup_{n \rightarrow \infty} \sum_{i=1}^{m_n} E \|Y_{ni}\|^2 \{ \|Y_{ni}\| > \eta \} = 0,$$

where  $\|\cdot\|$  is the Euclidean norm on  $\mathfrak{R}^d$ .

Then

- (i)  $\sum_{i=1}^{m_n} Y_{ni}$  converges weakly to  $Y_0 \sim N_d(0, V_0)$ ;  
 (ii) 
$$\sup_{h \in BL_1(\mathfrak{R}^d)} \left| E_z h \left( \sum_{i=1}^{m_n} z_i Y_{ni} \right) - E h(Y_0) \right| \rightarrow 0$$

in probability, as  $n \rightarrow \infty$ , where  $\mathfrak{R}^d$  is endowed with the uniform metric.

**Proof.** Part (i) follows from the Lindeberg–Feller central limit theorem. For part (ii), note that (a) and (b) together imply that both  $\sum_{i=1}^{m_n} \|Y_{ni}\|^2 \{ \|Y_{ni}\| > \eta \} \rightarrow 0$  and  $\sum_{i=1}^{m_n} Y_{ni} Y_{ni}^t \rightarrow V_0$  in probability, as  $n \rightarrow \infty$ , for every  $\eta > 0$ . This now implies that  $E_z \sum_{i=1}^{m_n} z_i^2 Y_{ni} Y_{ni}^t \rightarrow V_0$  also converges in probability. Fix  $\eta > 0$ . Since

$$\begin{aligned} E_z \sum_{i=1}^{m_n} z_i^2 \|Y_{ni}\|^2 \{ |z_i| \times \|Y_{ni}\| > \eta \} \\ \leq E_z (z_i^2 \{ |z_i| > k \}) \sum_{i=1}^{m_n} \|Y_{ni}\|^2 + k^2 \sum_{i=1}^{m_n} \|Y_{ni}\|^2 \{ \|Y_{ni}\| > \eta/k \}, \end{aligned}$$

for any positive  $k < \infty$ , we have that the left-hand side converges to zero in probability since we can choose  $k$  to make the first expectation on the right-hand side arbitrarily small. Since this is true for every  $\eta > 0$ , we can now replace  $\eta$  with a sequence  $\{\eta_n\}$  going to zero. Thus for every subsequence  $n'$ , there exists a further subsequence  $n''$  such that  $\lim_{n'' \rightarrow \infty} E_z \sum_{i=1}^{m_{n''}} z_i^2 Y_{n''i} Y_{n''i}^t = V_0$  and

$$\limsup_{n'' \rightarrow \infty} E_z \sum_{i=1}^{m_{n''}} z_i^2 \|Y_{n''i}\|^2 \{ |z_i| \times \|Y_{n''i}\| > \eta_{n''} \} = 0$$

almost surely. Thus, by the Lindeberg–Feller theorem combined with Theorem 1.12.2 of VW, we have with probability 1 that

$$\lim_{n'' \rightarrow \infty} \sup_{h \in BL_1(\mathfrak{R}^d)} \left| E_z h \left( \sum_{i=1}^{m_{n''}} z_i Y_{n''i} \right) - E h(Y_0) \right| = 0.$$

Since this is true for every subsequence  $n'$ , part (ii) follows by Lemma 1.9.2 of VW.  $\square$

**Proof of Theorem 2.** We will first apply Theorem 1 and Lemma 1 to the array  $\{z_i f_{ni}\}$  on the joint probability space defined above. Since

$$\sum_{i=1}^{m_n} z_i^2 [f_{ni}(\omega, s) - f_{ni}(\omega, t)]^2 \leq \left( \max_{1 \leq i \leq m_n} z_i^2 \right) \hat{\rho}_n^2(\omega, s, t),$$

we have that this triangular array is AMS. For vectors  $\mathbf{u} \in \mathfrak{R}^{m_n}$ , let  $|\mathbf{u}|$  denote pointwise absolute value and  $\text{sign}(\mathbf{u})$  denote pointwise sign. Now, for any nonnegative  $\alpha \in \mathfrak{R}^{m_n}$ ,

$$\begin{aligned} D_{m_n}(x || \alpha \odot |z_n| \odot F_n(\omega) ||, \alpha \odot z_n \odot \mathcal{F}_{n\omega}) \\ = D_{m_n}(x || \tilde{\alpha} \odot F_n(\omega) ||, \tilde{\alpha} \odot \text{sign}(z_n) \odot \mathcal{F}_{n\omega}) \\ = D_{m_n}(x || \tilde{\alpha} \odot F_n(\omega) ||, \tilde{\alpha} \odot \mathcal{F}_{n\omega}), \end{aligned}$$

where  $z_n \equiv \{z_1, \dots, z_{m_n}\}^T$ , since the absolute value of the  $\{z_i\}$  can be absorbed into the  $\alpha$  to make  $\tilde{\alpha}$  and since any coordinate change of sign does not effect the geometry of  $\mathcal{F}_{n\omega}$ . Thus the foregoing triangular array is manageable with envelopes  $\{|z_i|F_{ni}(\omega)\}$ .

Clearly,  $E\tilde{X}_{n\omega}(s)\tilde{X}_{n\omega}(t) = EX_n(s)X_n(t)$ ,  $\sum_{i=1}^{m_n} E^* z_i^2 F_{ni}^2 = \sum_{i=1}^{m_n} E^* F_{ni}^2$ , and

$$\left( \sum_{i=1}^{m_n} E z_i^2 |f_{ni}(\cdot, s) - f_{ni}(\cdot, t)|^2 \right)^{1/2} = \rho_n(s, t),$$

thus conditions (A), (B), (C') and (E) are satisfied. Now, for any  $\eta > 0$ , we have for any  $k > 0$  that

$$\begin{aligned} \sum_{i=1}^{m_n} E^* z_i^2 F_{ni}^2 \{|z_i|F_{ni} > \eta\} &\leq E(z_i^2 \{|z_i| > k\}) \sum_{i=1}^{m_n} E^* F_{ni}^2 \\ &+ k^2 \sum_{i=1}^{m_n} E^* F_{ni}^2 \{F_{ni} > \eta/k\}. \end{aligned}$$

Since the second term on the right-hand side goes to zero and the first term can be made arbitrarily small by choice of  $k$ , we have that condition (D') is also satisfied; and thus, by both Theorem 1 and Lemma 1,  $\tilde{X}_{n\omega}$  converges HJD weakly to the same limiting process  $X$  to which  $X_n$  converges. Hence  $\tilde{X}_{n\omega}$  is asymptotically measurable by Lemma 1.3.8 of VW.

We will now justify the lack of any outer expectation in (3.1). Fix  $h \in BL_1(\ell^\infty(T))$ . Clearly,  $h(X)$  is measurable by the fact that  $X$  is Borel measurable. Fix  $\omega \in \Omega$  and let  $\mathbf{a}, \mathbf{b} \in \mathfrak{R}^{m_n}$ , with  $\mathbf{a} = (a_1, \dots, a_{m_n})$  and  $\mathbf{b} = (b_1, \dots, b_{m_n})$ , and denote  $X_a^n(t) = \sum_{i=1}^{m_n} a_i(f_{ni}(\omega, t) - \mu_{ni}(t))$  and  $X_b^n(t) = \sum_{i=1}^{m_n} b_i(f_{ni}(\omega, t) - \mu_{ni}(t))$ . Then

$$|h(X_a^n) - h(X_b^n)|^2 \leq \sum_{i=1}^{m_n} (a_i - b_i)^2 \sum_{i=1}^{m_n} \left( \sup_{t \in T} |f_{ni}(\omega, t) - \mu_{ni}(t)| \right)^2,$$

implying that the set  $\{a \in \mathfrak{R}^{m_n} : h(X_a^n) \leq \alpha\}$  is the closure of a countable set for all  $\alpha \in \mathfrak{R}$ . Thus  $h(\tilde{X}_{n\omega})$  is a Borel measurable random variable on  $\{\Omega_z, \mathcal{W}_z, \Pi_z\}$ .

For each  $\delta > 0$ , let  $M_\delta$  assign to each  $t \in T$  a closest element of a given finite  $\delta$ -net for  $T$  with respect to  $\rho$ . Thus, by the fact that  $X$  concentrates on  $U_\rho(T)$ , we have that

$$\lim_{\delta \downarrow 0} \sup_{h \in BL_1(\ell^\infty(T))} |h(X(M_\delta(\cdot))) - h(X(\cdot))| = 0.$$

By Lemma 3, we next have that

$$\sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\tilde{X}_{n\omega}(M_\delta(\cdot))) - E h(X(M_\delta(\cdot)))| \rightarrow 0$$

in probability as  $n \rightarrow \infty$ . Now,

$$\begin{aligned} & \sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\tilde{X}_{n\omega}(M_\delta(\cdot))) - E_z h(\tilde{X}_{n\omega})| \\ & \leq \sup_{h \in BL_1(\ell^\infty(T))} E_z |h(\tilde{X}_{n\omega}(M_\delta(\cdot))) - h(\tilde{X}_{n\omega})| \\ & \leq E_z \left( \sup_{s, t \in T: \rho(s, t) \leq \delta} |\tilde{X}_{n\omega}(s) - \tilde{X}_{n\omega}(t)| \right)^* ; \end{aligned}$$

but the  $\limsup_{n \rightarrow \infty}$  of the expectation of this last term goes to zero, as  $\delta \downarrow 0$ , by the previously established unconditional weak convergence of  $\tilde{X}_{n\omega}$ . Thus the desired results follow.  $\square$

**Proof of Theorem 3.** For every  $t \in T$ ,

$$\begin{aligned} E_z [\hat{X}_{n\omega}(t) - \tilde{X}_{n\omega}(t)]^2 &= \sum_{i=1}^{m_n} [\hat{\mu}_{ni}(\omega, t) - \mu_{ni}(t)]^2 \\ &\rightarrow 0 \end{aligned}$$

in probability, as  $n \rightarrow \infty$ , thus also  $\hat{X}_{n\omega}(t) - \tilde{X}_{n\omega}(t)$  converges to zero in probability.

Now we will establish asymptotic tightness of  $\hat{X}_{n\omega}$ . Let  $\{r_n\}$  be a sequence going to zero. We have

$$\begin{aligned} & E_z \left( \sup_{s, t \in T: \rho(s, t) < r_n} \left| \sum_{i=1}^{m_n} z_i [\hat{\mu}_{ni}(\omega, t) - \mu_{ni}(t) - \hat{\mu}_{ni}(\omega, s) + \mu_{ni}(s)] \right| \right)^* \\ & \leq E_z \left( \sup_{s, t \in T: \rho(s, t) < r_n} \left| \sum_{i=1}^{m_n} z_i [\hat{\mu}_{ni}(\omega, t) - \hat{\mu}_{ni}(\omega, s)] \right| \right)^* \\ & \quad + E_z \left( \sup_{s, t \in T: \rho(s, t) < r_n} \left| \sum_{i=1}^{m_n} z_i [\mu_{ni}(t) - \mu_{ni}(s)] \right| \right)^* . \end{aligned} \tag{3.3}$$

However,

$$\begin{aligned} E^* & \left( \sup_{s,t \in T: \rho(s,t) < r_n} \left| \sum_{i=1}^{m_n} z_i [\mu_{ni}(t) - \mu_{ni}(s)] \right| \right) \\ & \leq E^* \left( \sup_{s,t \in T: \rho(s,t) < r_n} \left| \sum_{i=1}^{m_n} z_i [f_{ni}(\omega, t) - f_{ni}(\omega, s)] \right| \right) \\ & \rightarrow 0, \end{aligned}$$

as  $n \rightarrow \infty$ , by arguments used in the proof of Lemma 1. Thus the second term on the right-hand side of (3.3) goes to zero in probability as  $n \rightarrow \infty$ .

Now let

$$u'_n(\omega) \equiv r_n + \sup_{s,t \in T} (|\rho_n(s, t) - \rho(s, t)| + |\hat{\rho}_n(\omega, s, t) - \rho_n(s, t)|),$$

and note that

$$\limsup_{n \rightarrow \infty} \sup_{s,t \in T} |\rho_n(s, t) - \rho(s, t)| = 0$$

by condition (E) combined with the fact that  $\{T, \rho\}$  is totally bounded as a consequence of Theorem 1. Now,

$$\begin{aligned} E_z & \left( \sup_{s,t \in T: \rho(s,t) < r_n} \left| \sum_{i=1}^{m_n} z_i [\hat{\mu}_{ni}(\omega, t) - \hat{\mu}_{ni}(\omega, s)] \right| \right)^* \\ & \leq E_z \left( \sup_{s,t \in T: \hat{\rho}_n(\omega, s, t) < u'_n(\omega)} \left| \sum_{i=1}^{m_n} z_i [\hat{\mu}_{ni}(\omega, t) - \hat{\mu}_{ni}(\omega, s)] \right| \right) \\ & \leq E_z \left( \left[ 4 \sum_{i=1}^{m_n} z_i^2 \hat{F}_{ni}(\omega) \right]^{1/2} \right. \\ & \quad \times \Gamma \left( \frac{\sup_{s,t \in T: \hat{\rho}_n(\omega, s, t) < u'_n(\omega)} \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, t) - \hat{\mu}_{ni}(\omega, s)]^2}{4 \sum_{i=1}^{m_n} z_i^2 \hat{F}_{ni}^2(\omega)} \right)^* \\ & \equiv E_z R_n^*(\omega), \end{aligned}$$

where  $\Gamma$  is continuous and does not depend on  $\omega$  or  $n$ , with  $\Gamma(0) = 0$  and  $\Gamma(1) < \infty$ . The AMS condition gives us enough measurability so that we can use Fubini's theorem for the symmetrization arguments above (this is why no superscript-“\*” appears in the first term on the right-hand side of the above expression), but we otherwise need to be cautious.

Since

$$\begin{aligned} & \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, s) - \hat{\mu}_{ni}(\omega, t)]^2 \\ & \leq 3 \sum_{i=1}^{m_n} z_i^2 [\mu_{ni}(s) - \mu_{ni}(t)]^2 + 3 \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, s) - \mu_{ni}(s)]^2 \\ & \quad + 3 \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, t) - \mu_{ni}(t)]^2, \end{aligned}$$

we have

$$\begin{aligned} & \sup_{s, t \in T: \hat{\rho}_n(\omega, s, t) < u'_n(\omega)} \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, s) - \hat{\mu}_{ni}(\omega, t)]^2 \\ & \leq 3 \sup_{s, t \in T: \hat{\rho}_n(\omega, s, t) < u'_n(\omega)} \sum_{i=1}^{m_n} z_i^2 [\mu_{ni}(s) - \mu_{ni}(t)]^2 \\ & \quad + 6 \sup_{t \in T} \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, t) - \mu_{ni}(t)]^2. \end{aligned} \quad (3.4)$$

However, for every  $k_1 < \infty$ ,

$$\begin{aligned} & E_z \left( \sup_{t \in T} \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, t) - \mu_{ni}(t)]^2 \right) \\ & \leq k_1^2 \sup_{t \in T} \sum_{i=1}^{m_n} [\hat{\mu}_{ni}(\omega, t) - \mu_{ni}(t)]^2 \\ & \quad + E(z_1^2 \{|z_1| > k_1\}) \sum_{i=1}^{m_n} [\hat{F}_{ni}(\omega) + E_{\omega'}^* F_{ni}(\omega')]^2, \end{aligned} \quad (3.5)$$

where the last expectation is taken over a new copy of the probability space  $\{\Omega, \mathcal{W}, \Pi\}$ . The first term on the right-hand side of (3.5) goes to zero in probability by condition (G) while the second term can be made arbitrarily small by choice of  $k_1$  and the fact that

$$\sum_{i=1}^{m_n} [\hat{F}_{ni}(\omega) + E_{\omega'}^* F_{ni}(\omega')]^2 \leq 2 \sum_{i=1}^{m_n} \hat{F}_{ni}^2(\omega) + 2 \sum_{i=1}^{m_n} E_{\omega'}^* F_{ni}^2(\omega')$$

which is bounded in probability, as  $n \rightarrow \infty$ , by conditions (C') and (I). Thus the left-hand side of (3.5) goes to zero in outer probability as  $n \rightarrow \infty$ .

Now, for any  $\delta > 0$ ,

$$\begin{aligned} & \sup_{s,t \in T: \hat{\rho}_n(\omega, s, t) < u'_n(\omega)} \sum_{i=1}^{m_n} z_i^2 [\mu_{ni}(s) - \mu_{ni}(t)]^2 \\ & \leq \sup_{s,t \in T: \rho(s, t) < 2u'_n(\omega)} \sum_{i=1}^{m_n} z_i^2 [\mu_{ni}(s) - \mu_{ni}(t)]^2 \\ & \leq \{u'_n(\omega) < \delta/2\} \sup_{s,t \in T: \rho(s, t) < \delta} \sum_{i=1}^{m_n} z_i^2 [\mu_{ni}(s) - \mu_{ni}(t)]^2 \\ & \quad + \{u'_n(\omega) \geq \delta/2\} 4 \sum_{i=1}^{m_n} z_i^2 E_{\omega'}^* F_{ni}^2(\omega'); \end{aligned}$$

and the second term on the right-hand side goes to zero in probability by previous arguments, while

$$\begin{aligned} & E^* \left( \sup_{s,t \in T: \rho(s, t) < \delta} \sum_{i=1}^{m_n} z_i^2 [\mu_{ni}(s) - \mu_{ni}(t)]^2 \right) \\ & \leq E^* \left( \sup_{s,t \in T: \rho(s, t) < \delta} \sum_{i=1}^{m_n} z_i^2 [f_{ni}(\omega, s) - f_{ni}(\omega, t)]^2 \right) \end{aligned}$$

and thus the  $\limsup_{n \rightarrow \infty}$  of the entire right-hand side goes to zero as  $\delta \downarrow 0$ . Hence the left-hand side of (3.4) goes to zero in probability as  $n \rightarrow \infty$ .

For any  $\varepsilon > 0$ ,

$$\begin{aligned} E_z R_n^*(\omega) & \leq E_z \left( \left\{ \sum_{i=1}^{m_n} z_i^2 \hat{F}_{ni}^2(\omega) > \varepsilon \right\} R_n^*(\omega) + \left\{ \sum_{i=1}^{m_n} z_i^2 \hat{F}_{ni}^2(\omega) \leq \varepsilon \right\} R_n^*(\omega) \right)^* \\ & \leq E_z \left( \left\{ \sum_{i=1}^{m_n} z_i^2 \hat{F}_{ni}^2(\omega) > \varepsilon \right\} R_n^*(\omega) \right)^* + (4\varepsilon)^{1/2} \Gamma(1). \end{aligned}$$

The second term on the right-hand side can be made arbitrarily small by choice of  $\varepsilon$ ; but, for the first term on the right-hand side, we have

$$\begin{aligned} & E_z \left( \left\{ \sum_{i=1}^{m_n} z_i^2 \hat{F}_{ni}^2(\omega) > \varepsilon \right\} R_n^*(\omega) \right)^* \\ & \leq E_z \left( \left[ 4 \sum_{i=1}^{m_n} z_i^2 \hat{F}_{ni}^2(\omega) \right]^{1/2} \right. \\ & \quad \left. \times \Gamma \left( (4\varepsilon)^{-1} \sup_{s,t \in T: \hat{\rho}_n(\omega, s, t) < u'_n(\omega)} \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{ni}(\omega, s) - \hat{\mu}_{ni}(\omega, t)]^2 \right) \right)^* \end{aligned}$$

$$\leq \left( \left[ 4 \sum_{i=1}^{m_n} \hat{F}_{mi}^2(\omega) \right]^* \right)^{1/2} \times \left( E_z \Gamma^2 \left( (4\varepsilon)^{-1} \sup_{s,t \in T: \hat{\rho}_n(\omega, s, t) < u'_n(\omega)} \sum_{i=1}^{m_n} z_i^2 [\hat{\mu}_{mi}(\omega, s) - \hat{\mu}(\omega, t)]^2 \right)^* \right)^{1/2}.$$

Now the first term on the last line of the right-hand side is bounded in outer probability by condition (I) while the second term goes to zero in outer probability, as  $n \rightarrow \infty$ , by previous arguments combined with the bounded convergence theorem. Hence the left-hand side of (3.3) converges to zero in outer probability as  $n \rightarrow \infty$ , and thus

$$E_z \sup_{t \in T} |\hat{X}_{n\omega}(t) - \tilde{X}_{n\omega}(t)| \rightarrow 0 \quad (3.6)$$

in probability as  $n \rightarrow \infty$ . Thus  $\hat{X}_{n\omega}$  is asymptotically tight. Furthermore,

$$\begin{aligned} & \sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\hat{X}_{n\omega}) - Eh(X)| \\ & \leq \sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\tilde{X}_{n\omega}) - Eh(X)| + \sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\hat{X}_{n\omega}) - E_z h(\tilde{X}_{n\omega})|; \end{aligned}$$

but the first term on the right-hand side goes to zero by Theorem 2, while

$$\begin{aligned} & \sup_{h \in BL_1(\ell^\infty(T))} |E_z h(\hat{X}_{n\omega}) - Eh(\tilde{X}_{n\omega})| \leq E_z \sup_{t \in T} |\hat{X}_{n\omega}(t) - \tilde{X}_{n\omega}(t)| \\ & \rightarrow 0 \end{aligned}$$

in outer probability, as  $n \rightarrow \infty$ . The desired results now follow.  $\square$

#### 4. The two-parameter Cox score process

In this section, we apply the results of Section 3 to the two-parameter score process in a sequential clinical trial with staggered entry of patients. The two time parameters are the calendar time of entry and the time since entry for each patient. Sellke and Siegmund [13] made a fundamental breakthrough on this problem and important work on this problem has also been done by Slud [14] and Gu and Lai [6]. The most recent work on this problem, and the work upon which we will build, is that of Biliyas et al. [3] (hereafter abbreviated BGY).

For each patient, there is an entry time ( $\tau_i \geq 0$ ), a continuous failure time ( $X_i \geq 0$ ), a censoring time ( $C_i \geq 0$ ), and a real valued covariate process  $Z_i = \{Z_i(s), s \geq 0\}$ ,  $1 \leq i \leq n$ ,  $n \geq 1$ . Although the results we present are valid when  $Z_i$  is vector valued, we will assume that  $Z_i$  is scalar valued for simplicity. The entry time is on the calendar time scale while the remaining quantities are on the time since entry time scale. As is done in BGY, we will assume that the quadruples  $(\tau_i, X_i, C_i, Z_i)$ ,  $i = 1, \dots, n$ , are independent (but not identically distributed) and that the conditional hazard rate of  $X_i$  at  $s$ , give  $\tau_i$ ,  $C_i$ , and  $Z_i(u)$ , for  $u \leq s$ , has the Cox proportional hazards form

$\exp[\beta Z_i(s)]\lambda_0(s)$ , for some unknown baseline hazard  $\lambda_0$ . Thus, at calendar time  $x$ , the  $i$ th individual's failure time is censored at  $C_i \wedge (x - \tau_i)^+$ , where for a real number  $u$ ,  $u^+ = u\{u \geq 0\}$ . At any calendar time  $x$ , what we actually observe under possibly right-censoring is  $U_i(x) = X_i \wedge C_i \wedge (x - \tau_i)^+$  and  $\Delta_i(x) = \{X_i \leq C_i \wedge (x - \tau_i)^+\}$ . For  $x \geq s$ , denote  $N_i(x, s) = \Delta_i(x)\{U_i(x) \leq s\}$ ,  $Y_i(x, s) = \{U_i(x) \geq s\}$ , and

$$\bar{Z}(\beta; x, s) = \frac{\sum_{i=1}^n Z_i(s) \exp[\beta Z_i(s)] Y_i(x, s)}{\sum_{i=1}^n \exp[\beta Z_i(s)] Y_i(x, s)}.$$

The statistic of interest we will focus on is

$$W_n(x, s) = n^{-1/2} \sum_{i=1}^n \int_0^s [Z_i(u) - \bar{Z}(\beta_0; x, s)] N_i(x, du)$$

under the null hypothesis that  $\beta_0$  is the true value of  $\beta$  in the foregoing Cox proportional hazards model. For ease of exposition, we will assume throughout that  $\beta_0$  is known. It is easy to show that  $W_n(x, x)$  is the partial likelihood score at calendar time  $x$  and at  $\beta = \beta_0$ . When  $Z_i$  is a dichotomous treatment indicator,  $W_n(x, x)$  is the well known two-sample log-rank statistic and is a good choice for testing  $H_0: \beta = \beta_0$  versus  $H_A: \beta \neq \beta_0$ . However, for certain other alternative hypotheses, the supremum version of  $W_n$ ,  $\sup_{s \in (0, x]} |W_n(x, s)|$ , is a more powerful statistic (see [4]). Determining the asymptotic behavior of this last statistic requires weak convergence results whether continuous or group sequential interim monitoring is being done. Let  $D(x_0) = \{(x, s) : 0 \leq s \leq x \leq x_0\}$ , where  $x_0$  satisfies some assumptions given below. Under several assumptions, which we will review later, BGY demonstrate that  $W_n(x, s)$  converges HJD weakly in the uniform topology on  $\ell^\infty(D(x_0))$  to a tight mean zero Gaussian process  $W$  with a covariance which we will denote  $H$ .

Unfortunately, the complexity of the distribution of  $W$  precludes it from being used directly to compute critical boundaries, especially for the supremum version of the test statistic, during clinical trial execution. We will now show that the results of Section 3 can be used to obtain an asymptotically valid Monte Carlo estimate of the distribution of  $W$  for this purpose. We now present the assumptions given by BGY:

- (a)  $x_0 < \infty$  satisfies  $\liminf_{n \rightarrow \infty} n^{-1} \sum_{i=1}^n E Y_i(x_0, x_0) > 0$ ;
- (b) (Condition 1 in BGY) There exists a nonrandom  $B < \infty$  such that the total variation  $|Z_i(0)| + \int_0^{x_0} |Z_i(du)| \leq B$ ;
- (c) (Condition 2 in BGY) For  $k = 0, 1, 2$ , there exists  $\Gamma_k(x, s)$  such that, for all  $(x, s) \in D(x_0)$ ,

$$\lim_{n \rightarrow \infty} n^{-1} \sum_{i=1}^n E[Z_i^k(s) Y_i(x, s) \exp(\beta_0 Z_i(s))] = \Gamma_k(x, s);$$

- (d) (Condition 3 in BGY) Letting  $K(x, s) = \Gamma_1(x, s)/\Gamma_0(x, s)$  and

$$K_n(x, s) = \frac{\sum_{i=1}^n E[Z_i(s) Y_i(x, s) \exp(\beta_0 Z_i(s))]}{\sum_{i=1}^n E[Y_i(x, s) \exp(\beta_0 Z_i(s))]},$$



then, for each fixed  $s$ ,  $K(\cdot, s)$  is continuous on  $[s, x_0]$  and

$$\lim_{n \rightarrow \infty} \sup_{0 \leq x \leq x_0} \int_0^x [K_n(x, s) - K(x, s)]^2 ds = 0.$$

In the proof of their Theorem 2.2, BGY establish that  $W_n(x, s)$  converges in outer probability to  $\tilde{W}_n(x, s) = \sum_{i=1}^n f_{ni}(\omega, (x, s))$ , where

$$f_{ni}(\omega, (x, s)) = n^{-1/2} \int_0^s [Z_i(u) - K_n(x, u)] M_i(x, du), \quad (4.1)$$

$M_i(x, s) = N_i(x, s) - \int_0^s Y_i(x, u) \exp(\beta_0 Z_i(u)) \lambda_0(u) du$ ,  $\omega \in \Omega$ , and where the data for this statistic comes from the probability space  $\{\Omega, \mathcal{W}, \Pi\}$ . BGY establish that all of the conditions of Pollard's [10] functional central limit theorem are satisfied with measurable envelope functions, hence all of the conditions of Theorem 1 are satisfied, except for the “sufficient measurability” condition. It is actually not clear how all the necessary measurability conditions are addressed by BGY; however, it is not difficult to show that the inherent double right-continuity of both  $\tilde{W}_n(x, s)$  and all of the array components  $f_{ni}(\omega, (x, s))$  gives us separability (which implies AMS by Lemma 2) with  $T = D(x_0)$  and  $T_n = D(x_0) \cap [\mathcal{Q} \cup \{x_0\}]^2$ , where  $\mathcal{Q}$  is the set of rationals.

**Remark 4.** All of the conditions of Theorem 1 are thus satisfied and  $W_n$  converges HJD weakly to a tight, mean zero Gaussian process  $W$ . Consequently, if  $\{z_i, i \geq 1\}$  is a random sequence satisfying condition (F) and is independent of the data generating  $W_n$ , then the conditions of Theorem 2 are also satisfied. Thus the process  $\tilde{W}_n(x, s) \equiv \sum_{i=1}^{m_n} z_i f_{ni}(\omega, (x, s))$  is asymptotically tight, and

$$\sup_{h \in BL_1(\ell^\infty(D(x_0)))} |E_z h(\tilde{W}_n) - E h(W)| \rightarrow 0$$

in outer probability, as  $n \rightarrow \infty$ .

Since we usually do not have exact knowledge of either  $K_n$  or the  $M_i$ 's, we will need to find appropriate estimators and then apply Theorem 3 to obtain a Monte Carlo method of estimating the distribution of  $W$  based only on the data from the clinical trial. In this setting,  $\mu_{ni}((x, s)) = 0$ . However, if we use the estimator

$$\begin{aligned} \hat{\mu}_{ni}(\omega, (x, s)) = & n^{-1/2} \int_0^s [\bar{Z}(\beta_0; x, u) - K_n(x, u)] M_i(x, du) \\ & - n^{-1/2} \int_0^s [Z_i(u) - \bar{Z}(\beta_0; x, s)] \hat{M}_i(x, du), \end{aligned} \quad (4.2)$$

where

$$\hat{M}_i(x, du) = M_i(x, du) - Y_i(x, u) \exp(\beta_0 Z_i(u)) \frac{\sum_{j=1}^n M_j(x, du)}{\sum_{j=1}^n Y_j(x, u) \exp(\beta_0 Z_j(u))},$$

then

$$\begin{aligned} f_{ni}(\omega, (x, s)) - \hat{\mu}_{ni}(\omega, (x, s)) &= n^{-1/2} \int_0^s [Z_i(u) - \bar{Z}(\beta_0; x, u)] \hat{M}_i(x, du) \\ &= n^{-1/2} \int_0^s [Z_i(u) - \bar{Z}(\beta_0; x, s)] \\ &\quad \times \left[ N_i(x, du) - Y_i(x, u) \exp(\beta_0 Z_i(u)) \frac{\sum_{j=1}^n N_j(x, du)}{\sum_{j=1}^n Y_j(x, u) \exp(\beta_0 Z_j(u))} \right] \end{aligned}$$

can be computed from the data.

If we can next establish that the array  $\{\hat{\mu}_{ni}\}$  satisfies the conditions of Theorem 3, we will then have a Monte Carlo method of estimating the distribution of  $W$  based on the conditional distribution of the process

$$\hat{W}_n(x, s) = \sum_{i=1}^n z_i [f_{ni}(\omega, (x, s)) - \hat{\mu}_{ni}(\omega, (x, s))]$$

given the data from the clinical trial. To this end, we have the following theorem:

**Theorem 4.** *In the two-parameter Cox score process setting with staggered entry of patients with assumptions (a)–(d) satisfied, the triangular array of estimators  $\{\hat{\mu}_{ni}\}$ —of the form given in (4.2)—satisfies conditions (G)–(I) of Theorem 3.*

**Proof.** Because the processes  $\hat{\mu}_{ni}$  possess the same double right continuity that  $W_n$  possesses, the separability—and hence AMS—condition is readily satisfied. Because each  $\hat{\mu}_{ni}$  can be written as a difference between a monotone increasing and a monotone decreasing part with envelope  $\hat{F}_{ni}(\omega)$ , we have manageability since sums of monotone processes have pseudodimension one (see Lemma A.2 of BGY) and since sums of manageable processes are manageable. Since assumption (a) implies  $A_0(x_0) \equiv \int_0^{x_0} \lambda_0(u) du < \infty$  and also because of the bounded total variation of  $Z_i$ , we can use envelopes  $\hat{F}_{ni}(\omega) = \hat{C}n^{-1/2}$ , where there exists a  $k < \infty$  not depending on  $n$  such that  $\hat{C} \vee k$  converges in outer probability to  $k$  as  $n \rightarrow \infty$ . Hence conditions (H) and (I) of Theorem 3 are satisfied. All that remains to be shown is that  $\sup_{(t,s) \in T} \sum_{i=1}^n \hat{\mu}_{ni}^2(\omega, (x, s))$  converges to zero in outer probability.

Clearly,

$$\begin{aligned} & \sup_{(x,s) \in T} \sum_{i=1}^n \hat{\mu}_{ni}^2(\omega, (x, s)) \\ & \leq 2 \sup_{(x,s) \in T} n^{-1} \sum_{i=1}^n \left( \int_0^x [\bar{Z}(\beta_0; x, u) - K_n(x, u)] M_i(x, du) \right)^2 \\ & \quad + 2 \sup_{(x,s) \in T} n^{-1} \sum_{i=1}^n \left( \int_0^x [Z_i(u) - \bar{Z}(\beta_0; x, u)] Y_i(x, u) \exp(\beta Z_i(u)) \bar{M}(x, du) \right)^2, \end{aligned} \quad (4.3)$$

where

$$\bar{M}(x, du) \equiv \left[ \sum_{i=1}^n Y_i(x, u) \exp(\beta_0 Z_i(u)) \right]^{-1} \left[ \sum_{i=1}^n M_i(x, du) \right].$$

However, since  $\Lambda_0(x_0) < \infty$  and since  $M_i$  is the difference between two nonnegative monotone functions bounded by  $\Lambda_0(x_0)$ , the first term on the right-hand side of (4.3) is bounded by  $k_1 \sup_{(x,s) \in T} |\bar{Z}(\beta_0; x, s) - K_n(x, s)|^2$ , for some  $k_1 < \infty$ , thus this term vanishes in outer probability as  $n \rightarrow \infty$ . Using integration by parts combined with the fact that the total variation of  $Z_i$  is bounded, it can be shown that there exists constants  $c_1 < \infty$  and  $c_2 < \infty$  such that the second term on the right-hand side of (4.3) is bounded by

$$\begin{aligned} & \sup_{(x,s) \in T} n^{-1} \sum_{i=1}^n \left( 2c_1 \sup_{u \in [0,s]} |\bar{M}(x, u)| + 2c_2 \sup_{u \in [0,s]} \left| \int_0^u \bar{Z}(\beta_0; x, v) \bar{M}(x, dv) \right| \right)^2 \\ & \leq 4c_1^2 \sup_{(x,s) \in T} |\bar{M}(x, s)|^2 + 4c_2 \sup_{(x,s) \in T} \left| \int_0^s \bar{Z}(\beta_0; x, u) \bar{M}(x, du) \right|^2; \end{aligned}$$

and both of these terms can be shown to converge to zero in outer probability, as  $n \rightarrow \infty$ , by using arguments contained in BGY.  $\square$

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